

Application No. 09/747,521
Amendment dated August 12, 2003
Reply to Office action of May 7, 2003
Docket Number 22727/04079

Amendments to the Specification (Amendments made with reference to numbered paragraphs in Pub. No.: US 2002/0051791, Published on May 2, 2002)

Please replace paragraph [0015] with the following amended paragraph:

FIG. 3 shows the Plasmid pCI (Promega Inc.), the eukaryotic expression vector which was used to express aa amino acids 9-252 of the amino acid sequence shown in Figure 1B, i.e., amino acid 42 through amino acid 285 of SEQ ID NO. 2, of *B. anthracis* lethal factor protein, and aa amino acids 175-735 of the amino acid sequence shown in Figure 2B, i.e., amino acid 204 through amino acid 764 of SEQ ID NO. 4, of *B. anthracis* protective antigen protein.

Please amend Paragraph [0024] (lines 5-7), as indicated below:

... amino acid substitution of a glutamic acid for a ~~cysteine residue~~ cysteine residue at position 687 of the amino acid sequence shown in Figure 1B, i.e., amino acid 720 of SEQ ID NO. 2, or an immunogenic fragment thereof.

Please amend Paragraph [0026] (lines 9-11), as indicated below:

...except for a substitution of a glutamic acid for a cysteine at amino acid position 687 of the amino acid sequence shown in Figure 1B, i.e., amino acid 720 of SEQ ID NO. 2, has a sequence which is identical to the LF protein reference sequence.

Please amend Paragraph [0040] (lines 14-16), as indicated below:

... In one embodiment, the LF fragment polynucleotide comprises nucleotide ~~125~~ 124 through nucleotide 855 of the sequence, SEQ ID NO. 1, shown in Figure 1. ...

Please amend Paragraph [0061] (lines 4-5), as indicated below:

... pCLF4 encodes the LF protein fragment consisting of amino acids 9-252 of the amino acid sequence shown in Figure 1B, i.e., amino acid 42 through amino acid 285 of SEQ ID NO. 2, which includes the PA binding site. ...

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Please amend Paragraph [0062] (lines 6-8), as indicated below:

... protein which contains a mutation at position 687 (E687C) of the amino acid sequence shown in Figure 1B, i.e., amino acid 720 of SEQ ID NO. 2, in the zinc-binding active site thus eliminating the metalloproteinase activity of LF.

Please amend Paragraph [0073] (lines 3-4), as indicated below:

...The gene fragment encoding amino acids 175-735 of the amino acid sequence shown in Figure 2B, i.e., amino acid 204 through amino acid 764 of SEQ ID NO. 4, of the PA protein was PCR ...

Please amend Paragraph [0077] (lines 9-17), as indicated below:

... The pCPA plasmid expresses a truncated version of the PA gene product (aa 175-735 of the amino acid sequence shown in Figure 2B, i.e., amino acid 204 through amino acid 764 of SEQ ID NO. 4) which is the PA₆₃ antigen lacking the furin cleavage site (aa 164-167) yet is fully functional in vivo (Gordon 1995. Proteolytic activation of bacterial toxins by eukaryotic cells is performed by furin and by additional cellular proteases, Infect. Immun. 63:82-87.). The pCLF4 plasmid expresses a truncated form of LF (aa 9-252 of the amino acid sequence shown in Figure 1B, i.e., amino acid 42 through amino acid 285 of SEQ ID NO. 2) which lacks the catalytic domain of LF, yet retains PA₆₃ binding activity and is therefore capable of

Please amend Paragraph [0086] (lines 1-2), as indicated below:

Inducing a Protective Immune Response Against Challenge with *B. anthracis* ~~Seres~~ Spores by a Prime Boost Method